When is it Permissible to Administer Medications to Healthy Children in Research?

Effects of a Single Dose of Dextroamphetamine in ADHD: a Functional Magnetic Resonance Imaging Study

Background

- Attention Deficit Hyperactivity Disorder
  - Most common childhood behavioral disorder (5-10% of general population)
  - Core symptoms:
    - Difficulty paying attention
    - Inappropriate behavior
    - Impulsivity
  - Cause is unknown, genetic influence
  - Stimulants are the treatment of choice

Primary Scientific Questions

- Do children with ADHD have a different central nervous system response to stimulants (i.e., activation of fronto-striatal brain regions) compared to children without ADHD?
- Do genetic determinants or clinical characteristics predict CNS response patterns?

Scientific Value

Protocol: subjects

- 14 Children with ADHD
- 24 Monozygotic twins discordant for ADHD
- 24 Dizygotic twins discordant for ADHD
- 14 Healthy control children

- Age range for all children: 9-18 years

Protocol: procedures

- History and physical examination
- Blood work (including genetic testing)
- Neuropsychological testing
- Placebo-controlled, double-blinded administration of a single dose of dextroamphetamine (10 mg oral dose)
- Single functional MRI session (1-1.5 hrs)
- Subjects to be paid $ 570

IRB Concerns

- The primary IRB concern was about the risk level of the study for healthy children and whether the administration of a psychostimulant to these children (for whom there is no potential for medical benefit) was approvable under the federal regulations.
- Questions were also raised about the scientific value of the study
- Potential coercive effect of payment

Non-beneficial Pediatric Research

- The Federal Regulations allow IRBs to approve non-beneficial pediatric research provided the risks are no greater than minimal, defined as “the risks of daily life.”
- The regulations also allow IRBs to approve non-beneficial pediatric research provided that the study poses a “minor increment over minimal risk” and will yield “generalizable knowledge about the subject’s disorder or condition.”
- Non- beneficial research that poses more than a minor increment over minimal risk requires approval from DHHS (45 CFR 46.407 “panel”)

Risks of Study

- Evaluation
- Genetic testing
- fMRI
- Administration of dextramphetamine
  - Loss of appetite
  - Nervousness
  - Insomnia
  - Future substance abuse?

Stimulant Use in Children

- Risk of subsequent stimulant abuse
  - 3 of 4 studies found no association between stimulant treatment and an increased risk of future substance abuse in children with ADHD
  - No data are available relevant to risks associated with a single dose of a stimulant in healthy children